Exhibit 91

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Condom makers stop using talc

By MARIE MC CULLOUGH
KNIGHT-RIDDER NEWSPAPERS

Candace Sue Kasper believes "safe sex" should be as safe for women as for men.

So early this year, the Dallas skin pathologist began urging — some would say badgering — condom-makers and the federal Food and Drug Administration to stop the little-known practice of coating condoms with talc.

Talc, a powder made from the rock-like mineral magnesium silicate, is an excellent dry lubricant, but can scar soft tissues inside the body, where it does not dissolve. In women, body powders containing talc have been linked to infertility and ovarian cancer.

Kasper's campaign apparently worked.

"We've requested U.S. manufacturers to cease using (talc) and, in fact, all have agreed not to use it in manufacturing condoms," FDA spokesman Arthur Whitmore said last month.

Carter-Wallace, which makes Trojans and claims 60 percent of the American condom market, said in a statement that "to allay any possible concern," it has "discontinued the use of talc in its condom manufacturing process."

Talc, a powder made from the rock-like mineral magnesium silicate, is an excellent dry lubricant, but can scar soft tissues inside the body, where it does not dissolve. In women, body powders containing talc have been linked to infertility and ovarian cancer.

Kasper, 46, feels vindicated, but not victorious. She said an FDA official told her the agency had no rules against talc on condoms and no way to check compliance.

"When we have someone independent policing it, that's when I'll feel I have a victory," Kasper said.

Sales of condoms increased nearly 50 percent in the late 1980s, as AIDS awareness grew, according to the U.S. Centers for Disease Control and Prevention.

Kasper, an advocate of condom use, applauds the trend. And she is the first to say no research, including her own, has proved that talc specifically from condoms causes reproductive health problems in women.

Concern about talc as an ovarian carcinogen goes back 50 years in the medical literature. By the 1970s, evidence was mounting that talc particles might migrate into a woman's fallopian tubes where they could cause scarring and irritation of the ovaries. Scientists believed in some cases that the scarring led to infertility or cancer.

In 1992, Bernard Harlow, an epidemiologist and obstetrician-gynecologist at Harvard Medical School, published a study that found that women who used powder on their genitals, undergarments or diaphragms over a long period of time increased their risk of ovarian cancer threefold. (Today, feminine hygiene products use ingredients other than talc, though many baby and dusting powders still contain talc.)

Like Kasper, Harlow believes there is no reason to put talc on condoms — even if it has not been proven to be harmful — because cornstarch is a cheap, safe alternative.

"We'll probably never know for sure" that condom talc is unsafe, he said. "But why take the risk? Cornstarch does just fine and doesn't pose risks. I think it's prudent for manufacturers" to switch.

Indeed it is, said Ansell Inc. of Eatontown, which makes LifeStyle condoms and has about a quarter of the American condom market. Ansell switched from talc to cornstarch in January 1994.

"We knew surgical glove talc was a problem, so we figured there might be a problem with condoms," said Milt Hinsch, Ansell's vice president of technical affairs. "Whether it's rational or scientific, you just have to say, 'Let's not argue about it. Let's just do it.'"

In 1990, the FDA asked manufacturers to voluntarily stop putting talc on surgical gloves amid mounting scientific evidence that it caused adhesions in surgical patients. At the same time, the agency evaluated talc on condoms, but concluded the amount was insignificant and did not pose problems, said FDA spokeswoman Sharon Snider.

Kasper's concern about condoms arose after she and a colleague, Dallas plastic surgeon Preston Chandler, discovered talc in the hardened tissue surrounding breast implants that had been removed from women.

In a 1994 journal article, the two physicians speculated that the talc might have contributed to the hardening and that it came from surgical gloves. They also speculated that talc might play a role in the autoimmune symptoms that are the subject of numerous breast implant lawsuits.

Curious to see whether other products were dusted with talc, Kasper and Chandler bought condoms, pacifiers and baby-bottle nipples in 1994 at Dallas-area stores, then scrutinized them under a microscope. The nipples and pacifiers appeared clean, but all eight brands of American-made and foreign-made condoms had varying amounts of talc, cornstarch and, in some cases, substances such as sand, silicone dioxide or club moss spores (an outmoded lubricant that also causes scarring in soft tissues).

Kasper and Chandler wrote to the condom manufacturers, several of which responded that they did not use talc in their production process. Carter-Wallace did not respond to them, Kasper said.

Only one manufacturer, Ansell, backed up its claim to be talc-free, Kasper said. She examined Ansell condoms made after January 1994 and found cornstarch, not talc.

She and Chandler also expressed their concern to the FDA, which thanked them for their information — but didn't say it would take any action.

"Largely, we've been ignored," said Kasper, who has a private pathology practice and is a staff physician at Baylor Medical Center. "Fortunately, my livelihood doesn't depend on this. I've done this on my own time and money."

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American Health Consultants is A Medical Economics Company

You can steer clients to condoms free from potentially harmful talc

Condom companies agree to produce without the dry lubricant

Due to reports earlier this year that talc on condoms potentially could lead to infertility and ovarian cancer, some clinicians began warning clients to use only brands known to be talc-free. *Contraceptive Technology Update* recently contacted the major condom companies to determine if plant manufacturing processes had changed to eliminate talc, and all responded that, indeed, there is no longer talc on their condoms. They and other experts give you advice on how to counsel patients about finding talc-free condoms (see box, p. 135).

Some companies told us they didn't use talc at the time a letter to the editor of the *Journal of the American Medical Association* (*JAMA*) indicated the silicate had been found on their brands.[1] The authors of the letter stand behind their work and have provided *CTU* with copies of all correspondences between them and the companies, as well as with the U.S. Food and Drug Administration (FDA) in Rockville, MD.

Through the use of polarization microscopy, **Candace Sue Kasper**, MD, PhD, director of Southwest Dermatopathology Consultants in Dallas, and her colleague P.J. Chandler, MD, MBA, owner of Ambulatory Plastic Surgery Center, also in Dallas, showed that "maximum density" of talc particles could be found on the following:

- TrojanENZ nonlubricated condoms (Carter Wallace, Cranberry, NJ);
- Kimono lubricated condoms (Sagami Rubber, Tokyo/Mayer Laboratories, Oakland, CA);
- RIA lubricated condoms (Summa Trading Co., Malaysia).

They found "few to numerous" particles of talc in:

- Sagami lubricated condoms (Sagami Rubber/Mayer Laboratories);
- Lifestyle lubricated condoms (Ansell Consumer Products, Eatontown, NJ).

And they found "rare to few" particles in:

- Ramses Ultrathin condoms (London International U.S. Holdings, Sarasota, FL);
- Gold Circle Coin condoms (Aladan Corp., Norcross, GA).

The polarization examination, conducted with crossed filters that

block out light from all particles except those that are capable of bending light — like talc — was conducted during 1994. In addition to sending the results to *JAMA* at the end of 1994, Kasper sent them to the condom manufacturers and the FDA, she says. The letter appeared in *JAMA* on March 15, 1995.

David Mayer, president of Mayer Labs, a company that imports and distributes condoms in the United States, expressed surprise that talc had been found on the condoms he sells. He wrote to Kasper in January 1995 asking her to remove his condoms from the list of talc-containing products. Mayer attached a correspondence from Minoru Takahashi, director of the condom production division of Sagami Rubber, which makes Mayer's condoms under contract. Takahashi writes, "Sagami assures you that we never use the talc on all condoms manufactured by us as well as Kimono and Maxx series condoms to Mayer Laboratories."

After the *JAMA* letter appeared with Sagami/Mayer condoms still listed, Mayer wrote Kasper once again in May, stating, ". . . we require that you write a subsequent letter to *JAMA* informing the editor of the inaccuracy of your data and retracting the names of our products . . . ."

A "puzzled" Kasper responded in a letter that ". . . because we have confidence in our identification techniques, we see no reason to retract our findings. On the contrary, we think that it is you who needs to respond to us with full disclosure of the identity of all substances used in the manufacture and packaging of your condoms."

A more public exchange — letters from Mayer and Kasper — is due soon in *JAMA* but had not appeared at press time.

It has been almost 10 years since talc was used in the manufacturing of his company's condoms, Mayer tells *CTU*. He suggests the crystalline particles seen by Kasper are some other substance and not talc, but Kasper is dubious.

"There are some other crystals they might be, but it's unlikely," she says of the needle-like microscopic structures.

FDA: No talc on American condoms

After contacting the FDA in late 1994, Kasper says she was referred to the agency's division of compliance, where she learned that the condom companies could not be considered out of compliance because there were no guidelines about talc on condoms. Even if there were guidelines, they would apply only to new condoms, she was told.

Raju Kammula, PhD, DVM, the FDA's chief of toxicology, doesn't think the lack of guidelines is a problem since condom manufacturers are market-driven.

"The manufacturers comply voluntarily a lot of the time," he says. "They realize that if there's a problem and it's not corrected, their products won't be sold. I think this is one incentive they have. They want to promote a good product, and if there is any evidence that it is going to cause problems, their business will be affected."

Besides, guidelines aren't always necessary, since the site inspectors are trained to evaluate the manufacturing process, and talc is "something they can zero in on in a fairly straightforward manner," says **Colin Pollard**, chief of the FDA's OB/GYN devices branch. "Talc is an obvious part of the manufacturing process. It would be easy [for inspectors] to see." The inspectors also view "master files" of the manufacturing process kept by the companies and would notice talc immediately, he adds.

Site inspectors don't constantly keep tabs on plants in Japan and other foreign countries, but Pollard says the four U.S. manufacturers — London International (condoms are processed in Anderson, SC), Carter Wallace, Aladan, and Ansell — account for nearly 99% of the American market. All but Carter Wallace had indicated they stopped using talc prior to being contacted by the FDA, he says.

Ansell stopped using talc in January 1994 and began using a starch powder, according to a letter to Kasper from the company's vice president of technical affairs, J.W. Moushall. Moushall pointed out that talc levels prior to that were below 1% of all particles on the condom, based on results from Federal Bureau of Investigation (FBI) investigations of sex offenders who use condoms to avoid detection through semen analysis.

Carter Wallace last to switch

The FDA had subsequent discussions with Carter Wallace, "and as a result of that exchange, the company decided to take talc out of the [manufacturing] process," says Pollard.

One reason the company may have been reluctant to switch away from talc is because scientists there believed talc did not cause health problems. Based on presentations at a workshop co-sponsored by the FDA and the Columbia, MD-based International Society of Regulatory

Distribute the correct condoms at your facility

Now that you know the potential problems caused by talc on condoms, what should you do about it? Researchers who have been studying the possible health risks say you should simply choose the right condoms to distribute to your clients.

Candace Sue Kasper, MD, PhD, director of Southwest Dermatopathology Consultants in Dallas, is adamant that she doesn't want people to stop using condoms. Kasper simply wants condom manufacturers to use a substitute product that will work just as well as talc, such as corn starch. Family planning practitioners agree.

"It seems to me, if you have a choice, and one of the choices has unknown health risks, why use it?" asks **Dolly Joern**, ARNP, a clinician at Mount Vernon (WA) Women's Clinic.

Joern read reports linking condom use and talc exposure and began talking with patients about it. A "very relevant" topic for her since her mother and aunt both died of ovarian cancer, Joern has been suggesting to her clients that they use Lifestyles condoms.

Find companies that have announced their manufacturing system is free of talc and offer that company's condoms to clients, Kasper suggests. Lifestyles are a good choice, since the company was the first to acknowledge the need to switch to a different lubricant, she says.

All U.S. condom manufacturers have reportedly switched to other lubricants, such as corn starch or other types of food starch, says **Raju Kammula**, PhD, DVM, the Food and Drug Administration's chief of toxicology. Condoms made after March 1995 should be free from talc, he says.

The only problem that might arise is using condoms manufactured before the companies agreed to change their process. **David Mayer**, president of Mayer Labs, an Oakland, CA-based company that imports and distributes Kimono and Maxx brand condoms in the United States, also made two suggestions for clinicians and their patients. Since condoms manufactured before companies switched to new lubricants might still contain talc, he recommends checking all condom expiration dates. Choose ones with the dates most in the future; the normal expiration time is five years, so dates after 2000 should be free of talc.

When buying condoms in stores, shop where there would be a large volume of condoms purchased, Mayer says. This will ensure that the supplies are as fresh as possible. ■

Toxicology and Pharmacology in January 1994 called, "Talc: Consumer Uses and Health Perspectives," Carter Wallace issued a statement pointing out that:

- "studies . . . indicate the trace amounts of talc on a condom purchased by the consumer should present no known health concern";
- "the workshop concluded that when taken together, the results of these studies are insufficient to demonstrate any real association" between talc and ovarian tumors;
- ". . . there is no basis to conclude that talc is capable of migrating to the ovaries in the first place . . . ."

"That's what Carter Wallace wanted to come away with from [the workshop]. I didn't necessarily agree with that finding," says **Bernard L. Harlow**, PhD, a researcher in the OB/GYN epidemiology center of Brigham and Women's Hospital at Harvard Medical School in Boston. He presented a review of the scientific literature related to perineal talc exposure and the risk of ovarian cancer, which has recently been published.[2]

While Harlow says talc exposure may not be as big a risk factor for ovarian cancer as it once was, since women tend to use less talc applied directly to the perineum, new exposures — from condoms, for example — could change that scenario, he says.

The range of relative risk estimates in various studies of the association between ovarian cancer and perineal talc exposure is between 1.0 and 1.8,[1] which is plausible, says Harlow (1.0 would indicate no association; 2.0 would indicate a clear association).

"Many other risk factors contribute to the development of ovarian cancer much more so than perineal exposure to talc," he adds.

When it was found that tubal ligation was protective against ovarian cancer, researchers speculated it might be due to the inability of a carcinogen to travel up the tubes to the ovaries.[3] But the

Why is talc considered a problem substance?

Talc is a natural mineral, hydrous magnesium silicate in the asbestos family. Although it is a known sclerosing agent[1,2] and has been implicated as a lung carcinogen[3,4] and an ovarian carcinogen,[5-7] it is a prevalent substance in everyday life and can be found in everything from aspirin to cosmetics, says **Candace Sue Kasper**, MD, PhD, director of Southwest Dermatopathology Consultants in Dallas.

The "good, cheap lubricant" is safe as long as it doesn't come into contact with open tissue lesions, Kasper says. It is often used as a dry lubricant by the condom industry to facilitate the removal of dipped latex from the molds for foiling and filming packaging machines, and to keep the rolled condoms from sticking to each other before they can be packaged.

"As pathologists, we're very familiar with talc. It's not anything that's a mystery. We know what it looks like, we know what it does," says Kasper. "So talc is OK. But once it gets into the soft tissue, then it can cause a problem."

Talc doesn't harm people when it is ingested (unless they have ulcers or other open lesions in the digestive system), because peristalsis pushes it through the system and it has an exit. Therein lies the problem with the lungs and the ovaries.

"The difference with the ovary is that anything that gets up through the fallopian tube and passes to the ovary does not have an exit. There's nowhere for it to go," Kasper explains.

Talc can travel up the reproductive tract and sit on the surface of the ovary, she believes. When the ovary opens to release an egg, talc can get trapped inside. When the body mounts a defense and the talc is consumed by macrophages, cytokines are produced. It is these cytokines that can produce the fibrosis and scarring — and therefore infertility — talc has been associated with, Kasper says.

Kasper and her colleague P.J. Chandler, MD, MBA, of Ambulatory Plastic Surgery Center, also in Dallas, became interested in talc in 1989 when they were trying to determine why women's silicone breast implants sometimes made their breasts hard. At the time, Kasper worked at the University of Texas Southwestern Medical School in Dallas. A clinicopathologic study of the fibrotic capsules surrounding the implants turned up talc on 70% of the capsules,[8] probably from latex surgical gloves manufactured prior to 1991.[1] Curious about other latex products that might contain talc, they systematically purchased condoms, dental dams, baby bottle nipples, and pacifiers from local stores and began analyzing them under the microscope. While the baby products contained no talc, the condoms and the dental dams often did.[1]

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121,700 study subjects were asked about talc use on sanitary napkins or directly on the perineum. When analyzed, the relationship between talc exposure and ovarian cancer was not statistically significant, principal investigator **Susan Hankinson**, ScD, a researcher at Channing Laboratory in Boston, told *CTU* last year when her study was published.

(See *CTU*, May 1994, pp. 67-70.)

It would be difficult to compare perineal exposure and exposure from a condom, and even more difficult to measure talc exposure from condoms, Harlow says. Retrospectively, study subjects have trouble remembering how often they used condoms, much less if it was a brand that

had talc on it; a prospective study could not ethically expose a group of people to a substance that was potentially harmful.

Scientists at the Centers for Disease Control and Prevention (CDC) in Atlanta soon may be able to shed some light on the issue, however. During a recent preliminary review of an existing data set, no evidence for an association between those who had ever used a condoms and the risk for ovarian cancer could be found, says **Bert Peterson**, MD, chief of the women's health and fertility branch. Publication is pending, so details aren't available, but Peterson says the data set is large enough to generate meaningful evidence.

More studies needed

After conducting his extensive review, which he calls "the definitive paper on what we know about talc and where we need to go," Harlow concluded that more studies should be conducted to confirm or deny reports that talc can migrate and embed in human ovarian tissue. He was surprised to discover only two studies that investigated the issue, he says.

Kasper agrees more studies are needed. She would like to continue analyzing condoms for talc and other contaminants, but has left her position at the University of Texas Southwestern Medical School in Dallas and currently doesn't have easy access to the equipment she would need, she says. She did recheck a Lifestyles condom this summer, and it was free of talc.

She also recently rechecked a Ramses condom (which didn't have much talc to begin with) which still had high concentrations of lycopodium, a dry lubricant that comes from the spores of club moss, part of the fern family. In a statement to *CTU*, London International's Vice President of Marketing **John Blutenthal** writes: "London International U.S. Holdings Inc., makers of Ramses, Sheik, Touch, Avanti, and Fourex condoms, does not use talc or lycopodium in the manufacturing of its condoms."

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What are legalities of promoting ECPs?

Bottom line: It's 'defensible but risky'

Women should have wider access to emergency contraceptive pills (ECPs), an international group of experts recommended recently. But since the regimen involves using an approved drug for an unlabeled purpose, some providers worry they may be breaking the law by advertising or marketing the availability of the oral contraceptive (OC) pills for that purpose. Worse yet, some clinicians may be moving forward with highly visible marketing campaigns without knowing they are making themselves vulnerable to a battle in the courts.

Sometimes called postcoital or morning-after contraception, emergency methods include regular combined ethinyl estradiol/levonorgestrel pills given at a higher dose (the Yuzpe regimen) than normally prescribed and the copper IUD.

Because the legal boundaries about advertising emergency contraception have never been clear (see *Contraceptive Technology Update*, March 1993, pp. 33-45), *CTU* spoke with several lawyers to find out why. We learned that the basis for the law prohibiting the advertisement of unlabeled drugs is the 1938 Food, Drug, and Cosmetic Act and that the Food and Drug Administration (FDA) in Rockville, MD, does have authority to bring action against those who break the law. The FDA sets priorities regarding what issues will get the agency's attention, however.

In April, 24 experts representing the fields of research, policy, communications, women's advocacy, and medicine met in Bellagio, Italy, to discuss emergency contraception and made several recommendations. (See related article, p. 139.) They also ascertained the three reasons emergency contraception is not more widely available. They are:

- Women and providers are uninformed about the methods.
- Few products are marketed for emergency contraceptive use.
- Service providers are too often reluctant to provide the methods.

The meeting was held because many health care providers don't have an understanding of this important method of pregnancy prevention, says **Elizabeth Robinson**, associate director of

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Correction

In the September 1995 issue of *Contraceptive Technology Update*, the continuing education objectives inadvertently were omitted. Following are the continuing education nursing objectives for that issue:

1. Describe the reasons triphasic pills are prescribed in the clinic setting.
2. Cite the issues surrounding the over-the-counter oral contraceptive movement.
3. Describe the social and cultural effects of the Pill.
4. Counsel pill users about their risk for breast cancer.

CTU regrets the error. ■

Continuing education objectives

After reading this issue of *Contraceptive Technology Update*, the reader will be able to:

1. Describe the various Norplant implant removal techniques.
2. Find necessary resources to prepare for Norplant removals.
3. Cite several ways to better perform Norplant removals.
4. Describe how to counsel contraceptive patients about their risks for cardiovascular disease. ■

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Chudkowski, Michael

From: Christensen, Catherine
To: Chudkowski, Michael
Subject: Talc article
Date: Monday, October 23, 1995 9:28AM

October 23, 1995
WHY IS TALC CONSIDERED A PROBLEM SUBSTANCE?

Contraceptive Technology Update via First! : Talc is a natural mineral, hydrous magnesium silicate in the asbestos family. Although it is a known sclerosing agent1,2 and has been implicated as a lung carcinogen3,4 and an ovarian carcinogen,5-7 it is a prevalent substance in everyday life and can be found in everything from aspirin to cosmetics, says Candace Sue Kasper, MD, PhD, director of Southwest Dermatopathology Consultants in Dallas.
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First!

October 23, 1995

DISTRIBUTE THE CORRECT CONDOMS AT YOUR FACILITY

Contraceptive Technology Update via First! : Now that you know the potential problems caused by talc on condoms, what should you do about it? Researchers who have been studying the possible health risks say you should simply choose the right condoms to distribute to your clients.

Candace Sue Kasper, MD, PhD, director of Southwest Dermatopathology Consultants in Dallas, is adamant that she doesn't want people to stop using condoms. Kasper simply wants condom manufacturers to use a substitute product that will work just as well as talc, such as corn starch. Family planning practitioners agree.

"It seems to me, if you have a choice, and one of the choices has unknown health risks, why use it?" asks Dolly Joern, ARNP, a clinician at Mount Vernon (WA) Women's Clinic.

Joern read reports linking condom use and talc exposure and began talking with patients about it. A "very relevant" topic for her since her mother and aunt both died of ovarian cancer, Joern has been suggesting to her clients that they use Lifestyles condoms.

Find companies that have announced their manufacturing system is free of talc and offer that company's condoms to clients, Kasper suggests. Lifestyles are a good choice, since the company was the first to acknowledge the need to switch to a different lubricant, she says.

All U.S. condom manufacturers have reportedly switched to other lubricants, such as corn starch or other types of food starch, says Raju Kammula, PhD, DVM, the Food and Drug Administration's chief of toxicology. Condoms made after March 1995 should be free from talc, he says.

The only problem that might arise is using condoms manufactured before the companies agreed to change their process. David Mayer, president of Mayer Labs, an Oakland, CA-based company that imports and distributes Kimono and Maxx brand condoms in the United States, also made two suggestions for clinicians and their patients. Since condoms manufactured before companies switched to new lubricants might still contain talc, he recommends checking all condom expiration dates. Choose ones with the dates most in the future; the normal expiration time is five years, so dates after 2000 should be free of talc.

When buying condoms in stores, shop where there would be a large volume of condoms purchased, Mayer says. This will ensure that the supplies are as fresh as possible.

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First!

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YOU CAN STEER CLIENTS TO CONDOMS FREE FROM POTENTIALLY HARMFUL TALC

Contraceptive Technology Update via First! : Condom companies agree to produce without the dry lubricant

Due to reports earlier this year that talc on condoms potentially could lead to infertility and ovarian cancer, some clinicians began warning clients to use only brands known to be talc-free. Contraceptive Technology Update recently contacted the major condom companies to determine if plant manufacturing processes had changed to eliminate talc, and all responded that, indeed, there is no longer talc on their condoms. They and other experts give you advice on how to counsel patients about finding talc-free condoms (see box, p. 135).

Some companies told us they didn't use talc at the time a letter to the editor of the Journal of the American Medical Association (JAMA) indicated the silicate had been found on their brands.1 The authors of the letter stand behind their work and have provided CTU with copies of all correspondences between them and the companies, as well as with the U.S. Food and Drug Administration (FDA) in Rockville, MD.

Through the use of polarization microscopy, Candace Sue Kasper, MD, PhD, director of Southwest Dermatopathology Consultants in Dallas, and her colleague P.J. Chandler, MD, MBA, owner of Ambulatory Plastic Surgery Center, also in Dallas, showed that "maximum density" of talc particles could be found on the following:

- TrojanENZ nonlubricated condoms (Carter Wallace, Cranberry, NJ);
- Kimono lubricated condoms (Sagami Rubber, Tokyo/Mayer Laboratories, Oakland, CA);
- RIA lubricated condoms (Summa Trading Co., Malaysia).

They found "few to numerous" particles of talc in:

- Sagami lubricated condoms (Sagami Rubber/Mayer Laboratories);
- Lifestyle lubricated condoms (Ansell Consumer Products, Eatontown, NJ).

And they found "rare to few" particles in:

- Ramses Ultrathin condoms (London International U.S. Holdings, Sarasota, FL);
- Gold Circle Coin condoms (Aladan Corp., Norcross, GA).

The polarization examination, conducted with crossed filters that block out light from all particles except those that are capable of bending light - like talc - was conducted during 1994. In addition to sending the results to JAMA at the end of 1994, Kasper sent them to the condom manufacturers and the FDA, she says. The letter appeared in JAMA on March 15, 1995.

David Mayer, president of Mayer Labs, a company that imports and distributes condoms in the United States, expressed surprise that talc had been found on the condoms he sells. He wrote to Kasper in January 1995 asking her to remove his condoms from the list of talc-containing

products. Mayer attached a correspondence from Minoru Takahashi, director of the condom production division of Sagami Rubber, which makes Mayer's condoms under contract. Takahashi writes, "Sagami assures you that we never use the talc on all condoms manufactured by us as well as Kimono and Maxx series condoms to Mayer Laboratories."

After the JAMA letter appeared with Sagami/ Mayer condoms still listed, Mayer wrote Kasper once again in May, stating, ". . . we require that you write a subsequent letter to JAMA informing the editor of the inaccuracy of your data and retracting the names of our products . . . ."

A "puzzled" Kasper responded in a letter that ". . . because we have confidence in our identification techniques, we see no reason to retract our findings. On the contrary, we think that it is you who needs to respond to us with full disclosure of the identity of all substances used in the manufacture and packaging of your condoms."

A more public exchange - letters from Mayer and Kasper - is due soon in JAMA but had not appeared at press time.

It has been almost 10 years since talc was used in the manufacturing of his company's condoms, Mayer tells CTU. He suggests the crystalline particles seen by Kasper are some other substance and not talc, but Kasper is dubious.

"There are some other crystals they might be, but it's unlikely," she says of the needle-like microscopic structures.

FDA: No talc on American condoms

After contacting the FDA in late 1994, Kasper says she was referred to the agency's division of compliance, where she learned that the condom companies could not be considered out of compliance because there were no guidelines about talc on condoms. Even if there were guidelines, they would apply only to new condoms, she was told.

Raju Kammula, PhD, DVM, the FDA's chief of toxicology, doesn't think the lack of guidelines is a problem since condom manufacturers are market- driven.

"The manufacturers comply voluntarily a lot of the time," he says. "They realize that if there's a problem and it's not corrected, their products won't be sold. I think this is one incentive they have. They want to promote a good product, and if there is any evidence that it is going to cause problems, their business will be affected."

Besides, guidelines aren't always necessary, since the site inspectors are trained to evaluate the manufacturing process, and talc is "something they can zero in on in a fairly straightforward manner," says Colin Pollard, chief of the FDA's OB/GYN devices branch. "Talc is an obvious part of the manufacturing process. It would be easy [for inspectors] to see." The inspectors also view "master files" of the manufacturing process kept by the companies and would notice talc immediately, he adds.

Site inspectors don't constantly keep tabs on plants in Japan and other foreign countries, but Pollard says the four U.S. manufacturers - London International (condoms are processed in Anderson, SC), Carter Wallace, Aladan, and Ansell - account for nearly 99% of the American market. All but Carter Wallace had indicated they stopped using talc prior to being contacted by the FDA, he says.

Ansell stopped using talc in January 1994 and began using a starch powder, according to a letter to Kasper from the company's vice president of technical affairs, J.W. Moushall. Moushall pointed out that talc levels prior to that were below 1% of all particles on the condom, based on results from Federal Bureau of Investigation (FBI) investigations of sex offenders who use condoms to avoid detection through semen analysis.

Carter Wallace last to switch

The FDA had subsequent discussions with Carter Wallace, "and as a result of that exchange, the

company decided to take talc out of the [manufacturing] process," says Pollard.

One reason the company may have been reluctant to switch away from talc is because scientists there believed talc did not cause health problems. Based on presentations at a workshop co-sponsored by the FDA and the Columbia, MD- based International Society of Regulatory Toxicology and Pharmacology in January 1994 called, "Talc: Consumer Uses and Health Perspectives," Carter Wallace issued a statement pointing out that:

- "studies . . . indicate the trace amounts of talc on a condom purchased by the consumer should present no known health concern";
- "the workshop concluded that when taken together, the results of these studies are insufficient to demonstrate any real association" between talc and ovarian tumors;
- ". . . there is no basis to conclude that talc is capable of migrating to the ovaries in the first place . . . ."

"That's what Carter Wallace wanted to come away with from [the workshop]. I didn't necessarily agree with that finding," says Bernard L. Harlow, PhD, a researcher in the OB/GYN epidemiology center of Brigham and Women's Hospital at Harvard Medical School in Boston. He presented a review of the scientific literature related to perineal talc exposure and the risk of ovarian cancer, which has recently been published.2

While Harlow says talc exposure may not be as big a risk factor for ovarian cancer as it once was, since women tend to use less talc applied directly to the perineum, new exposures - from condoms, for example - could change that scenario, he says.

The range of relative risk estimates in various studies of the association between ovarian cancer and perineal talc exposure is between 1.0 and 1.8,1 which is plausible, says Harlow (1.0 would indicate no association; 2.0 would indicate a clear association).

"Many other risk factors contribute to the development of ovarian cancer much more so than perineal exposure to talc," he adds.

When it was found that tubal ligation was protective against ovarian cancer, researchers speculated it might be due to the inability of a carcinogen to travel up the tubes to the ovaries.3 But the 121,700 study subjects were asked about talc use on sanitary napkins or directly on the perineum. When analyzed, the relationship between talc exposure and ovarian cancer was not statistically significant, principal investigator Susan Hankinson, ScD, a researcher at Channing Laboratory in Boston, told CTU last year when her study was published. (See CTU, May 1994, pp. 67-70.)

It would be difficult to compare perineal exposure and exposure from a condom, and even more difficult to measure talc exposure from condoms, Harlow says. Retrospectively, study subjects have trouble remembering how often they used condoms, much less if it was a brand that had talc on it; a prospective study could not ethically expose a group of people to a substance that was potentially harmful.

Scientists at the Centers for Disease Control and Prevention (CDC) in Atlanta soon may be able to shed some light on the issue, however. During a recent preliminary review of an existing data set, no evidence for an association between those who had ever used a condoms and the risk for ovarian cancer could be found, says Bert Peterson, MD, chief of the women's health and fertility branch. Publication is pending, so details aren't available, but Peterson says the data set is large enough to generate meaningful evidence.

More studies needed

After conducting his extensive review, which he calls "the definitive paper on what we know about talc and where we need to go," Harlow concluded that more studies should be conducted to confirm or deny reports that talc can migrate and embed in human ovarian tissue. He was

surprised to discover only two studies that investigated the issue, he says.

Kasper agrees more studies are needed. She would like to continue analyzing condoms for talc and other contaminants, but has left her position at the University of Texas Southwestern Medical School in Dallas and currently doesn't have easy access to the equipment she would need, she says. She did recheck a Lifestyles condom this summer, and it was free of talc.

She also recently rechecked a Ramses condom (which didn't have much talc to begin with) which still had high concentrations of lycopodium, a dry lubricant that comes from the spores of club moss, part of the fern family. In a statement to CTU, London International's Vice President of Marketing John Blutenthal writes: "London International U.S. Holdings Inc., makers of Ramses, Sheik, Touch, Avanti, and Fourex condoms, does not use talc or lycopodium in the manufacturing of its condoms."

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WHY IS TALC CONSIDERED A PROBLEM SUBSTANCE?

Contraceptive Technology Update via First! : Talc is a natural mineral, hydrous magnesium silicate in the asbestos family. Although it is a known sclerosing agent1,2 and has been implicated as a lung carcinogen3,4 and an ovarian carcinogen,5-7 it is a prevalent substance in everyday life and can be found in everything from aspirin to cosmetics, says Candace Sue Kasper, MD, PhD, director of Southwest Dermatopathology Consultants in Dallas.

The "good, cheap lubricant" is safe as long as it doesn't come into contact with open tissue lesions, Kasper says. It is often used as a dry lubricant by the condom industry to facilitate the removal of dipped latex from the molds for foiling and filming packaging machines, and to keep the rolled condoms from sticking to each other before they can be packaged.

"As pathologists, we're very familiar with talc. It's not anything that's a mystery. We know what it looks like, we know what it does," says Kasper. "So talc is OK. But once it gets into the soft tissue, then it can cause a problem."

Talc doesn't harm people when it is ingested (unless they have ulcers or other open lesions in the digestive system), because peristalsis pushes it through the system and it has an exit. Therein lies the problem with the lungs and the ovaries.

"The difference with the ovary is that anything that gets up through the fallopian tube and passes to the ovary does not have an exit. There's nowhere for it to go," Kasper explains.

Talc can travel up the reproductive tract and sit on the surface of the ovary, she believes. When the ovary opens to release an egg, talc can get trapped inside. When the body mounts a defense and the talc is consumed by macrophages, cytokines are produced. It is these cytokines that can produce the fibrosis and scarring - and therefore infertility - talc has been associated with, Kasper says.

Kasper and her colleague P.J. Chandler, MD, MBA, of Ambulatory Plastic Surgery Center, also in Dallas, became interested in talc in 1989 when they were trying to determine why women's silicone breast implants sometimes made their breasts hard. At the time, Kasper worked at the University of Texas Southwestern Medical School in Dallas. A clinicopathologic study of the fibrotic capsules surrounding the implants turned up talc on 70% of the capsules,8 probably from latex surgical gloves manufactured prior to 1991.1 Curious about other latex products that might contain talc, they systematically purchased condoms, dental dams, baby bottle nipples, and pacifiers from local stores and began analyzing them under the microscope. While the baby products contained no talc, the condoms and the dental dams often did.1

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